REMARKS

STATUS OF CLAIMS

The Office Action Summary (of paper no. 13) indicates that all pending claims (*i.e.*, 1, 5, 9, 17, 22, 45-51, 53-63, 65-75) are rejected. However, no rejection is presented of claims 54, 57, 66, and 69. Moreover, paragraph no. 16, at page 9 of the office action (paper no. 13) provides a statement of reasons for the indication of allowable subject matter. Applicant believes that claims 54, 57, 66, and 69 are considered allowable by the examiner. Applicants request that the examiner clarify this discrepancy.

OBVIOUSNESS-TYPE DOUBLE PATENTING

Applicants appreciate the withdrawal of the rejection for obviousness-type double patenting.

REJECTION OF CLAIMS 1, 5, 9, 17, 22, 45-51, 53, 55-56, 58-63, and 70-75 UNDER 35 U.S.C. §112, FIRST PARAGRAPH

The enumerated claims are rejected as being directed to generic methods that are not supported adequately by the species disclosed in the specification. This rejection is respectfully traversed.

The Manual of Patent Examining Procedure sets forth the standard for a rejection for lack of adequate written description (§2163):

> A description as filed is presumed to be adequate, unless or until sufficient evidence or reasoning to the contrary has been presented by the examiner to rebut the presumption. *See, e.g., In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971). The examiner, therefore, must have a reasonable basis to challenge the adequacy of the written description. The examiner has the initial burden of presenting by a preponderance of evidence why a person skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims. *Wertheim*, 541 F.2d at 263, 191 USPQ at 97.

The Patent Office has failed to meet its burden because it has failed to present any evidence at all why a person skilled in the art would not recognize that the disclosure described the invention defined by the claims.

The Patent Office alleges that the claims are generic and inadequately described in the following aspects:

- any virus
- any ligand
- any means of expressing a ligand on a virus surface.

However, it has not indicated why one of ordinary skill in the art would not be able to recognize that any virus, ligand, or means of viral surface expression could be used. Those of skill in the art are aware of many viruses, ligands, and means of expressing ligands on virus surfaces. Information which is well known in the art need not be described in detail in the specification. See, e.g., *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379-80, 231 USPQ 81, 90 (Fed. Cir. 1986). The Patent Office has not presented any reasons why any of the known viruses, ligands, or means of expressing ligand on virus surfaces could not be used in the claimed methods.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species. See *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406. In some cases one species adequately supports a genus. *See, e.g., Rasmussen*, 650 F.2d at 1214, 211 USPQ at 326-27; *In re Herschler*, 591 F.2d 693, 697, 200 USPQ 711, 714 (CCPA 1979) (disclosure of corticosteroid in DMSO held sufficient to support claims drawn to a method of using a mixture of a "physiologically active steroid" and DMSO); *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 285 (CCPA 1973). Description

of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces. M.P.E.P. § 2163. The Patent Office has not set forth why the species it acknowledges as being adequately described (*e.g.*, Mag 4.1 and Mag 4.2) are not representative of the entire claimed genus.

The Office Action has pointed to the working examples which describe the use of bacteriophage vectors expressing Mag proteins as fusion proteins in bacteriophage and the use of the bacteriophage for detecting NMDA receptors. However, the Patent Office has failed to assess the rest of the specification which indeed supports a generic scope for the claims. In the opening paragraph of the Detailed Description, the applicants describe the invention as being of the same scope as the claims:

> The present invention provides a method of detecting the presence of a polypeptide in a sample comprising contacting with the sample a detectable virus expressing on its surface a ligand for the polypeptide and detecting binding of the virus to the sample, thus detecting the presence of the polypeptide in the sample.

Page 6, lines 3-6. The disclosure is not limited to any specific virus, specific ligand, or specific means of expressing on a virus particle. The generic scope of the invention is further supported in the disclosures of the individual components utilized in the claimed method. The virus as disclosed can be any virus:

> The virus utilized in the method can be a bacteriophage. For example the bacteriophage can be bacteriophage f1, M13, and other bacteriophages known in the art. *Viruses can include any other desired virus, as will be recognized by those of skill in the art, such as adenovirus, etc.* The phage or virus can be modified in any of various ways known in the art, such as to be rendered replication-deficient or to eliminate other viral genes, and methods of such modifications are standard in the art.

Page 7, lines 1-6 (emphasis added). The generic scope of the invention is further supported in the description of the means of expressing on a viral particle surface. There is no indication that any

particular means is required:

> The virus is modified to express the ligand on the surface of the virus, as by engineering the virus genome to encode a fusion protein for a coat protein and the ligand. For example, in bacteriophage, the ligand can be encoded by pIII or pVIII protein. Making bacteriophage that express peptides on their surface is standard in the art (described in e.g., U.S. Pat No. 5,427,908; U.S. Pat No. 5,403,484; U.S. Pat No. 5,432,018; U.S. Pat No. 5,432,018; U.S. Pat No. 5,270,170; WO 92/06176; Smith et al. (1993); Kolvunen, E. et al., J. Cell Biol. 124:373 (1994); Kolvunen, E. et al., Meth. Enzymol. 245:346 (1994); Pasqualini, R et al. J Cell Biol. 130:1189 (1995)).

Page 7, lines 6-14. The generic scope of the invention is further supported in the description of the ligand. There is no limit on the ligand which can be used:

> A ligand can be previously determined to specifically bind the selected protein by any known, standard means for determining such binding or, for example, as described herein. A ligand can include, for example, a peptide hormone, a toxin, a fragment from a large protein.

Page 8, lines 7-10. In sum, there is absolutely no indication that the applicants disclosed and described an invention that was any more narrow than the claims.

Because the Patent Office has failed to meet its burden in making a *prima facie* case of inadequate written description, and because the specification describes the invention as being of the same scope as the claims, the rejection should be withdrawn.

REJECTION OF CLAIMS 1, 5, 9, 17, AND 22 UNDER 35 U.S.C. §112, FIRST PARAGRAPH

The enumerated claims are rejected for containing new matter: the recitation "homogenous population" allegedly has no clear support in the specification. Moreover, the recitation allegedly broadens the scope of the invention. These two allegations are respectfully traversed.

Support for a new claim recitation does not require that the recitation appear in the specification *in haec verba* (in the same words). Rather, the newly added claim recitation can be

supported in the specification through express, implicit, or inherent disclosure. M.P.E.P § 2163.

The use of a homogenous population of virus expressing on its surface a ligand for the polypeptide is amply supported throughout the specification as a whole. The specification implicitly teaches the notion of a homogenous population of virus at the following particular locations:

> Page 3, line 18-21 ("In search of novel peptides that modulate receptor activity, **phage clones with specific interacting peptides from random peptide libraries have been isolated** by panning selection, which is often based on the multivalent interaction between the phage particle and target receptor.")
>
> Page 11, lines 1-3 ("**Virus or phage compositions can include various amounts of the selected virus** in combination with a pharmaceutically acceptable carrier and, in addition, if desired, may include other medicinal agents, pharmaceutical agents, carriers, adjuvants, diluents, etc.")
>
> Page 12, lines 4-5 ("The examples herein show **the isolation of a phage clone** carrying a low affinity peptide, which specifically recognizes truncated NMDA receptor fragment.")
>
> Page 12, lines 24-25 ("Monitoring receptor expression using **recombinant bacteriophage with specific peptide ligands** shares several advantages of other immnunoassays.")
>
> Page 14 lines 20-23 (" After five consecutive rounds of selection and amplification, **clones that specifically bind N-NR1 fusion protein were identified** by testing the binding of **individual phage clone** to the immobilized N-NR1 (phage ELISA) (Barrett et al., 1992).")

It is clear from these quotations that the specification is directed to the use of isolated virus clones that specifically recognize a particular protein. These are not libraries of clones but single clones that can be isolated from libraries. Isolated clones inherently form a homogenous population. It is respectfully submitted that the phrase "homogenous population" does not constitute new matter, but rather it specifies what is inherently disclosed in the specification as originally filed. Withdrawal of this rejection is therefore respectfully requested.

REJECTION OF CLAIMS 1, 5, 9, 45-51, 53, 55-56 UNDER 35 U.S.C. §102(b)

Shatz (U.S. 5,270,120) is cited as anticipating claims 1, 5, 9, 45-51, 53, 55-56.

In order to find anticipation, each and every element set forth in the claim must be found in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of California*, 2 U.S.P.Q. 2d 1051, 1053 (Fed. Cir. 1987). Shatz does not teach each element and thus fails to anticipate the claims.

The rejected claims recite:

- a homogeneous population of detectable virus expressing a ligand on its surface;
- contacting a sample with the detectable virus;
- detecting binding of the virus to the sample.

First, Shatz does not employ a homogeneous population of virus expressing a ligand on its surface. Shatz employs a library of mixed identities. The Office Action does not dispute this distinction between Shatz and the pending claims. It merely ignored it because it characterized the distinguishing recitation in the claims as "new matter." As demonstrated above, the use of a homogenous population is inherently disclosed in the application as originally filed. Thus this recitation should not be discounted and should be considered as sufficient to distinguish the present claims over Shatz.

Second, Shatz' invention does not employ a detectable **virus expressing a ligand on its** surface. Shatz is cited as teaching the use of plasmids or phage vectors which express fusion products. See column 4, lines 42-48. Shatz, however, does not teach a virus with a ligand expressed on its surface.

Third, Shatz does not teach the steps of **contacting a virus with a sample** and detecting the presence of a polypeptide in the sample **by virus binding to the sample**. Shatz screens a library of heterogeneous peptides by binding them to a receptor and isolating the

peptide from the library that binds to the receptor. The Office Action points to Shatz's teaching that a particular peptide can be identified and used as the basis for developing a diagnostic assay. Office Action, paper no. 13, at page 8, lines 3-4. Shatz teaches: "Once a peptide has been identified, that peptide can serve as, or provide the basis for, the development of a vaccine, a therapeutic agent, a diagnostic reagent, etc." Column 5, lines 25-28. However, nowhere does Schatz teach that the diagnostic assay would employ a virus particle which expresses the particular peptide on its surface. There is no teaching or suggestion in Schatz of using this type of diagnostic assay rather than the multitudes of diagnostic assays known in the art.

Shatz fails to teach all elements of the claims. Therefore, Shatz does not anticipate the rejected claims.

REJECTION OF CLAIMS 1, 5, 9, 17, 22, 45-51, 53, 55-56, 58-63, 65, 67-68, and 70-75 UNDER 35 U.S.C. §103(a)

The enumerated claims are rejected as unpatentable over a combination of Shatz (U.S. 5,270,170) and Barbas, III (U.S. 6,242,568).

"To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations." M.P.E.P. §2143. The rejection of the enumerated claims over Shatz and Barbas, III, fails to make a *prima facie* case because the prior art references fail to teach or suggest all the claim limitations.

Each of the rejected claims recites "a homogeneous population of detectable virus expressing a ligand on its surface." As detailed above, Shatz does not teach this element of the claimed methods. Moreover, Barbas, III, does not remedy this deficiency. Barbas is cited by the Patent Office merely to teach that fact that pVIII coat protein is expressed in multiple copies. This teaching clearly does not remedy the deficiency of Shatz in teaching an assay which uses a homogenous population of detectable virus expressing a ligand on its surface, *i.e.,* the surface of a viral particle. Since neither reference teaches this element the combination of references *per force* fails to teach this element. On this basis alone the rejection fails to meet the Patent Office's own requirements for making a *prima facie* case. In view of this failure, the rejection should be withdrawn.

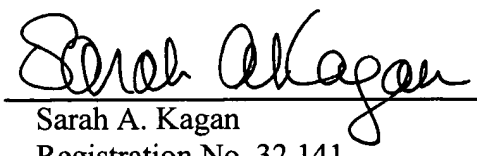
CONCLUSION

All rejections having been addressed, applicant respectfully submits that the instant application is in condition for allowance, and respectfully solicits prompt notification of the same.

Respectfully submitted,

BANNER & WITCOFF, LTD.

Dated: March 29, 2004

By: 

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